

**AMENDMENTS TO THE CLAIMS:**

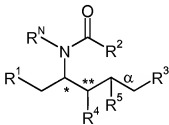
Please amend the claims as follows:

Claims 1-91. (Canceled)

92. (Currently Amended) A pharmaceutical formulation suitable for parenteral administration comprising:

(i) an amphiphilic drug selected from the group consisting of an anthracycline and an alkaloid; and

(ii) a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R<sup>1</sup> is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R<sup>1</sup> is independently:

an O-linked (optionally N-(C<sub>1-6</sub>alkyl)-substituted

amino)-C<sub>1-6</sub>alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C<sub>1-6</sub>alkyl-  
phosphate group;

R<sup>2</sup> is independently C<sub>3-9</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>3</sup> is independently C<sub>7-19</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>4</sup> is independently -H, -OH, or -O-C<sub>1-4</sub>alkyl;

R<sup>N</sup> is independently -H or C<sub>1-4</sub>alkyl;

the bond marked with an alpha ( $\alpha$ ) is independently a  
single bond or a double bond;

if the bond marked with an alpha ( $\alpha$ ) is a double bond, then R<sup>5</sup> is -H;

if the bond marked with an alpha ( $\alpha$ ) is a single bond, then R<sup>5</sup> is -H or -OH;

the carbon atom marked (\*) is independently in an R-configuration or an  
S-configuration;

the carbon atom marked (\*\*) is independently in an R-configuration or an  
S-configuration;

with the proviso that when R<sup>1</sup> is an O-linked saccharide group which is derived  
from galactopyranose, then R<sup>1</sup> is D-galactopyranosyl- $\beta$ 1-;

and pharmaceutically acceptable salts thereof.

Claim 93. (Canceled)

94. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is an anthracycline.

95. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: doxorubicin, idarubicin, epirubicin, aclarubicin, mitrozantrone, and daunorubicin, and salts thereof.

96. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is doxorubicin or doxorubicin hydrochloride.

97. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is an alkaloid.

98. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: topotecan and camptothecin.

99. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is linear.

100. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is linear; and has from 0 to 3 carbon-carbon double bonds.

101. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is unsubstituted or substituted with from 1 to 3 substituents selected from  $C_{1-4}$ alkyl, -OH,  $C_{1-4}$ alkoxy,  $-C(=O)OH$ , and  $-C(=O)O-C_{1-4}$ alkyl.

102. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is  $-(CH_2)_nCH_3$ , wherein n is an integer from 4 to 8.

103. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is  $-(CH_2)_nCH_3$ , wherein n is an integer from 6 to 8.

104. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^2$  is  $-(CH_2)_6CH_3$ .

105. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a double bond and  $R^5$  is -H.

106. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a single bond; and  $R^5$  is -H.

107. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a single bond; and  $R^5$  is -OH.

108. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^3$  is linear.

109. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^3$  is linear; and has from 0 to 3 carbon-carbon double bonds.

110. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^3$  is unsubstituted or substituted with from 1 to 3 substituents selected from  $C_{1-4}$ alkyl, -OH,  $C_{1-4}$ alkoxy.

111. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^3$  is  $-(CH_2)_nCH_3$ , wherein n is an integer from 8 to 16.

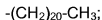
112. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^3$  is  $-(CH_2)_{12}CH_3$ .

113. (Previously Presented) A pharmaceutical formulation according to claim 92,  
 wherein the moiety:



is selected from the following:

- (CH<sub>2</sub>)<sub>8</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>10</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>12</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>14</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>7</sub>-CH=CH-(CH<sub>2</sub>)<sub>5</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>16</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>7</sub>-CH=CH-(CH<sub>2</sub>)<sub>7</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>9</sub>-CH=CH-(CH<sub>2</sub>)<sub>5</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>7</sub>-[CH=CH-CH<sub>2</sub>]<sub>2</sub>-(CH<sub>2</sub>)<sub>3</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>7</sub>-[CH=CH-CH<sub>2</sub>]<sub>3</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>4</sub>-[CH=CH-CH<sub>2</sub>]<sub>3</sub>-(CH<sub>2</sub>)<sub>3</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>7</sub>-[CH=CH]<sub>3</sub>-(CH<sub>2</sub>)<sub>3</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>18</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>6</sub>-[CH=CH-CH<sub>2</sub>]<sub>2</sub>-(CH<sub>2</sub>)<sub>6</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>3</sub>-[CH=CH-CH<sub>2</sub>]<sub>3</sub>-(CH<sub>2</sub>)<sub>6</sub>-CH<sub>3</sub>;
- (CH<sub>2</sub>)<sub>3</sub>-[CH=CH-CH<sub>2</sub>]<sub>4</sub>-(CH<sub>2</sub>)<sub>3</sub>-CH<sub>3</sub>;



analog of the foregoing wherein the left-most  $-(\text{CH}_2)_{20}-$  is replaced with  $-\text{CH}=\text{CH}-$ ; and

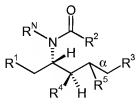
analog of the foregoing wherein the left-most  $-(\text{CH}_2)-$  is replaced with  $-\text{CH}(\text{OH})-$ .

114. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $\text{R}^4$  is -H, -OH, -OMe, -OEt, -O(iPr), -O(nPr), -O(nBu), -O(iBu), -O(sBu), or -O(tBu).

115. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $\text{R}^4$  is -OH.

116. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $\text{R}^N$  is -H, -Me, or -Et.

117. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the carbon atoms marked (\*) and (\*\*) have a configuration as shown in the following formula:



118. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $\text{R}^1$  is an O-linked saccharide group.

119. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> is an O-linked mono-, di-, or tri-saccharide group.

120. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> comprises a group or groups selected from:

arabinose, lyxose, ribose, xylose,

allose, altrose, glucose, mannose, gulose, idose, galactose, and

talose;

and derivatives thereof.

121. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> is an O-linked mono-, di-, or tri-saccharide group comprising a group or groups selected from:

arabinose, lyxose, ribose, xylose,

allose, altrose, glucose, mannose, gulose, idose, galactose, talose,

sucrose, maltose, lactose, cellobiose, galabiose,

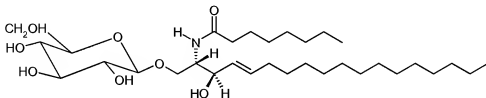
globotriaose, isoglobotriaose, mucotriaose, lactotriaose,

neolactotriaose gangliotriaose, galatrinaose, mollutriaose, and antrotriaose;

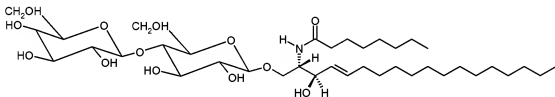
and derivatives thereof.

122. (Previously Presented) A pharmaceutical formulation according to claim 120, wherein said saccharide group derivatives are selected from deoxy, di-deoxy, di-deoxy-di-dehydro, methoxy, acetoxo, carboxylic acid, sulfuric acid, amino-deoxy, N-acetyl-amino-deoxy, or N-sulfo-amino-deoxy.

123. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula (C<sub>8</sub>-GlcCer):

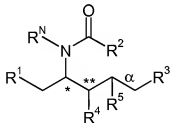


124. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula:



125. (Previously Presented) A pharmaceutical formulation comprising:

- (i) a drug; and
- (ii) a short-chain sphingolipids selected from compounds of the following formula



wherein:

R<sup>1</sup> is independently an O-linked polyhydric alcohol group

R<sup>2</sup> is independently C<sub>3-9</sub>alkyl,

and is independently unsubstituted or substituted;



$R^3$  is independently  $C_{7-19}$ alkyl,

and is independently unsubstituted or substituted;

$R^4$  is independently -H, -OH, or  $-O-C_{1-4}$ alkyl;

$R^N$  is independently -H or  $C_{1-4}$ alkyl;

the bond marked with an alpha ( $\alpha$ ) is independently a

single bond or a double bond;

if the bond marked with an alpha ( $\alpha$ ) is a double bond, then  $R^5$  is -H;

if the bond marked with an alpha ( $\alpha$ ) is a single bond, then  $R^5$  is -H or -OH;

the carbon atom marked (\*) is independently in an R-configuration or an S-configuration;

the carbon atom marked (\*\*) is independently in an R-configuration or an S-configuration;

and pharmaceutically acceptable salts thereof.

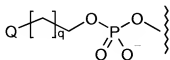
126. (Previously Presented) A pharmaceutical formulation according to claim 125, wherein  $R^1$  comprises a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

127. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein  $R^1$  is:

an O-linked (optionally N-( $C_{1-4}$ alkyl)-substituted amino)- $C_{1-6}$ alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)- $C_{1-6}$ alkyl-phosphate group.

128. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> is:



wherein:

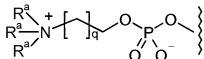
q is an integer from 0 to 5;

Q is: -NH<sub>2</sub>, -NHR<sup>a</sup>, -NR<sup>a</sup><sub>2</sub>, or -NR<sup>a</sup><sub>3</sub><sup>+</sup>; or:

Q is a polyhydric alcohol group, linked via an oxygen atom;

each R<sup>a</sup> is linear or branched saturated C<sub>1-4</sub>alkyl.

129. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> is:

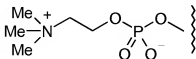


wherein:

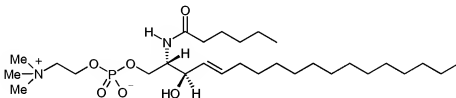
q is an integer from 0 to 5; and

each R<sup>a</sup> is a C<sub>1-4</sub>alkyl group.

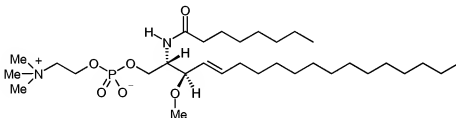
130. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R<sup>1</sup> is:



131. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula ("C<sub>6</sub>-SM"):



132. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula ("3-O-methyl-C<sub>8</sub>-SM"):



133. (Previously Presented) A pharmaceutical formulation according to claim 128, wherein Q is a polyhydric alcohol group, linked via an oxygen atom.

134. (Previously Presented) A pharmaceutical formulation according to claim 133, wherein Q comprises a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

Claim 135. (Canceled)

136. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the pharmaceutical formulation is a liposomal pharmaceutical formulation.

137. (Previously Presented) A liposomal pharmaceutical formulation according to claim 136, wherein the liposomes of the liposomal pharmaceutical formulation are prepared using a mixture of lipids comprising, at least, vesicle-forming lipids and said short-chain sphingolipid.

138. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids and said short-chain sphingolipid.

139. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids, cholesterol, and said short-chain sphingolipid.

140. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phosphatidylcholines, cholesterol, and said short-chain sphingolipid.

141. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises fully hydrogenated soy phosphatidylcholine (HSPC), cholesterol, and said short-chain sphingolipid.

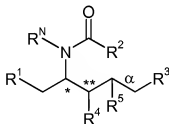
142. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises dipalmitoyl-phosphatidylcholine (DPPC), cholesterol, and said short-chain sphingolipid.

143. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a vesicle-forming lipid which is derivatized with a polymer chain.

144. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG).

145. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG2000-DSPE).

146. (Currently Amended) A pharmaceutical formulation according to claim 92, in the form of Caelyx® or Doxil® liposomes post-inserted with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R<sup>1</sup> is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R<sup>1</sup> is independently:

an O-linked (optionally N-(C<sub>1-4</sub>alkyl)-substituted amino)-C<sub>1-6</sub>alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C<sub>1-6</sub>alkyl-phosphate group;

R<sup>2</sup> is independently C<sub>3-9</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>3</sup> is independently C<sub>7-19</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>4</sup> is independently -H, -OH, or -O-C<sub>1-4</sub>alkyl;

R<sup>N</sup> is independently -H or C<sub>1-4</sub>alkyl;

the bond marked with an alpha (α) is independently a single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R<sup>5</sup> is -H;

if the bond marked with an alpha (α) is a single bond, then R<sup>5</sup> is -H or -OH;

the carbon atom marked (\*) is independently in an R-configuration or an S-configuration;

the carbon atom marked (\*\*) is independently in an R-configuration or an S-configuration;

with the proviso that when R<sup>1</sup> is an O-linked saccharide group which is derived from galactopyranose, then R<sup>1</sup> is D-galactopyranosyl-β1-;

and pharmaceutically acceptable salts thereof.

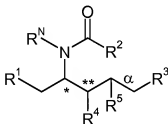
Claims 147-151. (Canceled)

152. (new) A pharmaceutical formulation suitable for parenteral administration comprising:

(i) a drug; and

(ii) a short-chain sphingolipid selected from compounds of the following

formula:



wherein:

R<sup>1</sup> is independently an O-linked polyhydric alcohol group;

R<sup>2</sup> is independently C<sub>3-9</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>3</sup> is independently C<sub>7-19</sub>alkyl,

and is independently unsubstituted or substituted;

R<sup>4</sup> is independently -H, -OH, or -O-C<sub>1-4</sub>alkyl;

R<sup>N</sup> is independently -H or C<sub>1-4</sub>alkyl;

the bond marked with an alpha (α) is a single bond;

R<sup>5</sup> is -H or -OH;

the carbon atom marked (\*) is independently in an R-configuration or an S-configuration;

the carbon atom marked (\*\*) is independently in an R-configuration or an S-configuration;

and pharmaceutically acceptable salts thereof.

153. (new) A pharmaceutical formulation suitable for parenteral administration comprising:

(i) an amphiphilic drug; and

(ii) a short-chain sphingolipid having the following formula ("3-O-methyl-C<sub>8</sub>-SM"):

